REMARKS

Regarding the rejection of claims 9-11 as being anticipated by either Adleman, Guarnieri, or Oliver, under 35 USC 102(b):

Lines 20-21 of claim 9 are amended to recite that the claimed method comprises "obtaining a composition comprising at least one set of single-stranded oligomers E_i and $\underline{E}_i$ representing the components of a vector, said composition comprising an oligomer representing a vector component with a positive amplitude and also comprising an oligomer representing a vector component with a negative amplitude, ..."

Support for this amendment is found in the specification in lines 1-4 of page 5, where the invention is described as providing a "method for DNA-based analog representation of the operations of vector addition and vector and matrix algebra, using negative as well as non-negative numbers;" and in lines 4-15 of page 5, which describe representing positive and negative amplitudes of each vector component with concentrations of an oligonucleotide strand or its complement, respectively, that are proportional to the amplitude values. Similarly, lines 5-13 of page 27 describes the invention as providing a means for representing both positive and negative amplitudes: "Since DNA concentrations are always positive, an appropriate representation for negative amplitudes is needed [10]. In the present invention, negative amplitudes associated with unit vectors $\boldsymbol{e}_i$ are represented by DNA oligomers $\underline{E}_i$ having a nucleotide sequence complementary to E_i. As a result, when two vectors are added, any positive and negative amplitudes will hybridize, and the resulting double-stranded DNA oligomers can be removed from the set of single-stranded DNA molecules." In addition, descriptions of specific operations carried out according to the present invention, such as vector addition (see p. 29, lines 21-23), and obtaining the outer product of two vectors (see p. 32, line 20, to p. 33, line 17),

describe operations using a composition comprising a set of single-stranded oligomers E_i and $\underline{E}_i$ representing the components of a vector, where the composition comprises an oligomer representing a vector component with a positive amplitude and also comprises an oligomer representing a vector component with a negative amplitude, as recited in the amended claim. The last line of claim 9 is also be amended by replacing the second instance of E_i with $\underline{E}_i$, to correct a formal error. The Applicants submit that amended claim 9 does not contain new matter.

Applicants further submit that amended claim 9 is not anticipated by the methods described in the cited prior art references, because these methods do not utilize complementary oligomers to represent input values of mixed sign.

Adleman's method uses oligonucleotides for molecular computation to find solutions to combinatorial problems. The method involves obtaining a set of oligomers, each of which represents either a "vertex" of a graph, or an "edge" that connects two vertices of the graph. Corresponding vertex and edge oligomers have complementary portions, as illustrated in Figs. 1 and 2 on page 1022 of the reference. Pooling oligomers representing selected edges and vertices results in hybridization of the complementary portions of edge and vertex oligomers, and the length of the resulting hybrid structure, detectable by gel electrophoresis, reveals the Hamiltonian path between the vertices (see Fig. 3 on p. 1023). The path problem solved by Adleman's method does not call for input values of mixed sign, and Adleman does not describe a method that operates on input values of mixed sign.

Likewise, neither Guarnieri nor Oliver disclose methods for operating on values of opposite sign. Guarnieri describes his method as "a general algorithm for DNA-based addition of any two nonnegative rational binary numbers." See the first complete paragraph on page 221.

Oliver expressly states that his method is limited to non-negative input values in lines 1-3 of the abstract ("[a] DNA-based method for calculating the product of Boolean matrices or matrices containing positive, real numbers is presented"), and in the first complete paragraph in the right column of page 165 ("[m]ultiplication of matrices containing nonnegative real numbers can be achieved using DNA of the transmission factors are encoded by the concentrations of DNA representing the edges.")

In view of the above, Applicants respectfully request withdrawal of the rejection of claims 9-11 under 35 USC 102(b), as being anticipated by either Adleman, Guarnieri, or Oliver.

Regarding the rejection of claim 11 for containing new matter:

Claim 11 is amended by deleting the words "in an enzyme-catalyzed reaction" from section (i) to remove the generic phrase that the Examiner has indicated is lacking support. Line 16 of claim 11 is also amended by re-designating section (k) as section (j), to correct the informality of having skipped (j) in the recited steps. Applicants submit that amended claim 11 does not contain new matter, and respectfully request that rejection of claim 11 be withdrawn.

Regarding rejection of claim 15 for non-enablement under 35 USC 112, 1st paragraph:

Claim 15 is amended to be an independent claim; and in accordance with this change, lines 4 and 5 of claim 15 are amended to describe the oligomers E_i and $\underline{E}_i$ as initially recited in claim 9, from which claim 15 formerly depended. Claim 15 is further amended by changing "j = 1 to j = n" in lines 11 and 12 to "j = 1, 2, ..., n," so that the form of indexing of W_j in lines 11 and 12 agrees with the form of indexing of W_j stated in lines 3-4 of claim 15. In addition to providing consistency in the form of indexing used in the claim, the amendment conforms the

form if indexing used in the claim to that used in the description of a generic vector in lines 10 and 12 of page 26 of the specification. The last three lines of claim 15 are also amended to recite that the concentration of each dimeric oligomer, which comprises oligomer sequences corresponding to the i-th component of ***V*** and the j-th component of **W**, is proportional to the product of the amplitudes of the i-th component of ***V*** and the j-th component of **W**. This feature of a set of dimeric oligomers that are an analog representation of an outer product matrix is described in the specification in lines 14-16 of page 35: "The number of ij strands is proportional to the product of the concentrations of the V_i and W_j strands and hence to the desired outer product." A biochemical approach to making a set of dimeric oligomers that represents an outer product matrix is described in the specification from line 20 of page 33 to line 14 of page 35. The specification also teaches that, "The oligomers of the present invention can be made by well-known methods that are routinely used by those skilled in the art of synthesizing oligonucleotides and/or oligonucleotide analogs [citations omitted]" (see the paragraph bridging pages 14-15). Having the detailed description of a set of dimeric oligomers that are an analog representation of an outer product matrix that is set out in claim 15, one skilled in the art would be able to make the claimed invention by following the biochemical procedures described on pages 33-35, or by synthesizing the oligonucleotides de novo as taught on pages 14-15, without undue experimentation. The Applicants respectfully submit that amended claim 15 satisfies the enablement requirement of 35 USC 112, first paragraph, and does not contain new matter.

Regarding the rejection of claim 17 for containing new matter:

The Applicants respectfully submit that amended claim 17 does not contain new matter, because equation of the saturating strands with the E_i and $\underline{E}_i$ strands as recited in claim 17 is fully supported by the original specification. Applicants acknowledge that lines 18-20 of page 48 and lines 14-16 of page 49 support the recitation that the X_i strands are hybridized to a sub-stoichiometric set of E_i and E_i strands, but that, taken alone and out of context, they do not expressly equate the E_i and E_i strands to the saturating strands. However, the equation of the E_i and E_i strands and the saturating strands is clearly indicated in the specification by the following lines of text that follow immediately after the designated lines on page 48:

(i) Line 21 of page 48 to line 3 of page 49 state that, the "set of E_i and $\underline{E}_i$ strands used to apply the saturating function can be anchored to a solid support ... or they can be free in solution, e.g. with each *saturating oligomer* being linked to a ligand or an additional oligomer to facilitate isolation of the set of X_i strands selected by the saturating reaction.

(ii) Lines 3-11 of page 49 further describe the method step as one in which "[t]he unhybridized, single-stranded X_i strands are then washed away or are otherwise separated from the double-stranded complexes formed by hybridizing the X_i strands to the set of *saturating E_i and $\underline{E}_i$ strands*...." (Italicization added for emphasis)

Passage (i) above clearly equates the set of E_i and $\underline{E}_i$ strands with the saturating oligomers, and the passage (ii) above refers to the saturating oligomers as the set of saturating E_i and $\underline{E}_i$ strands. Accordingly, Applicants respectfully submit that there is express support in the specification for the equation of the set of E_i and $\underline{E}_i$ strands with the saturating oligomers as recited in claim 17.

Claim 24 is amended to depend on claim 23 instead of itself, in correction of an obvious typographical error.

Respectfully submitted,

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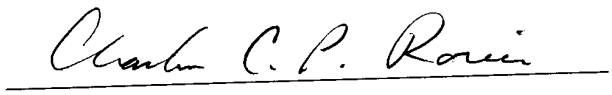

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